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TUMOR DEVELOPED FROM ABERRANT ADRENAL IN THE KIDNEY.

By Thos. S. Cullen, M. B., *Assistant Resident Gynecologist, The Johns Hopkins Hospital.*

[*Read before the Johns Hopkins Medical Society.*]

H. J., æt. 49, German. Admitted in the service of Dr. Kelly, October 10th, 1894. Her complaint on entrance was pain in the lower part of the abdomen associated with swelling in the lower abdominal region. Her menses commenced at twelve and ceased six years ago. She has been married twenty-eight years and has had two children. Her family history is unimportant. Twelve years ago she had malaria, and for several years she has complained of frequent micturition.

Her present trouble commenced in May, 1894, when she noticed a swelling in the lower part of the abdomen. This has gradually increased and has been associated with a moderate amount of discomfort rather than actual pain. The swelling seems to be located on the right side.

Status præsens. The patient is apparently well nourished, but slightly debilitated. Her appetite is poor, her tongue flabby but clean, bowels regular. The urine has S. G. 1030, is amber colored, gives an acid reaction and contains a faint trace of albumen, and microscopically shows a few pus cells.

The abdominal measurements are as follows: Girth at umbilicus 100 cm., just above pubes 103 cm.; distance from pubes to umbilicus, 19.5 cm.; from ensiform cartilage to umbilicus, 19.5 cm.; from right superior spine to umbilicus, 23 cm.; from left ant. superior spine to umbilicus, 23 cm. To the left of the umbilicus there is slight flattening, to the right moderate bulging, and 6 cm. to the right of the umbilicus a distinct tumor can be felt.

Operation, October 11th, by Dr. Kelly. Incision was made in the median line under the supposition that the tumor was an ovarian cyst, as with the patient in the standing position it lay in the right iliac fossa and crossed over the median line just above the symphysis. On opening the abdomen the tumor was found to be retroperitoneal, and could not be reached on account of the excessive amount of fat. An oblique incision 12 cm. long was made midway between the lower border of the ribs and the crest of the ilium, and commencing posteriorly at the quadratus lumborum. A soft tumor was exposed and punctured on the supposition that it contained fluid. From the point of puncture free bleeding occurred, but no fluid escaped. The incision was enlarged by cutting upward and inward toward the ensiform cartilage. In doing this the peritoneal cavity was opened. Considerable difficulty was experienced in enucleating the tumor from its bed of adipose tissue. The ureter as well as the large vessels at the hilum of the kidney were tied off by about eight stout ligatures. A small gauze drain was introduced into the posterior angle of the wound, the peritoneum closed by silk sutures, the muscle and skin by silkworm-gut. The stitches were removed on October 19th. The patient made a good

recovery and was discharged on November 10th. The average temperature for the first ten days was 99.5°. Soon after the operation it dropped to 96°, but the same evening rose again.

Pathological Report.

The specimen consists of the right kidney, the lower half of which is of normal size, being 12 cm. long, 6 broad, and 5 in its antero-posterior diameter. It presents several fœtal lobulations. The upper half, however, is greatly enlarged and the seat of a neoplasm. This part has an oval contour, is 18x18 x12 cm. in its various diameters, is covered with adipose tissue, and has a fibrous capsule which is directly continuous with the capsule of the kidney; thus it is apparent that the new growth has developed in the kidney. The tumor presents a yellowish mottling, and in the depth of the capsule numerous branching blood-vessels can be seen. On pressure it is yielding and elastic. On section the new growth presents a mottled appearance, the prevailing color being yellow. The consistence of the outer part of the growth is moderately firm, that of the central portion is soft, and evidently here and there is extensive necrosis with some hæmorrhage. At one point the tumor extends into the pelvis in the form of a pyramidal growth, evidently corresponding in shape and position to one of the renal pyramids (see Fig. 1). This tongue-like process of the tumor is 2.5 cm. long and 2 cm. broad, and projects free into the pelvis of the kidney, which it partially occludes. This projection shows no degeneration. The capsule of the tumor is directly continuous with the capsule of the kidney, and a layer of renal substance can be traced partly over the tumor beneath the capsule, indicating that the tumor has developed in the substance of the kidney (Fig. 1). Scattered throughout the capsule are numerous blood-vessels which appear as narrow slits. Extending inward from the capsule are trabeculæ which can be traced to the very centre of the tumor, where they are seen as delicate fibrils. The lower half of kidney shows no apparent change.

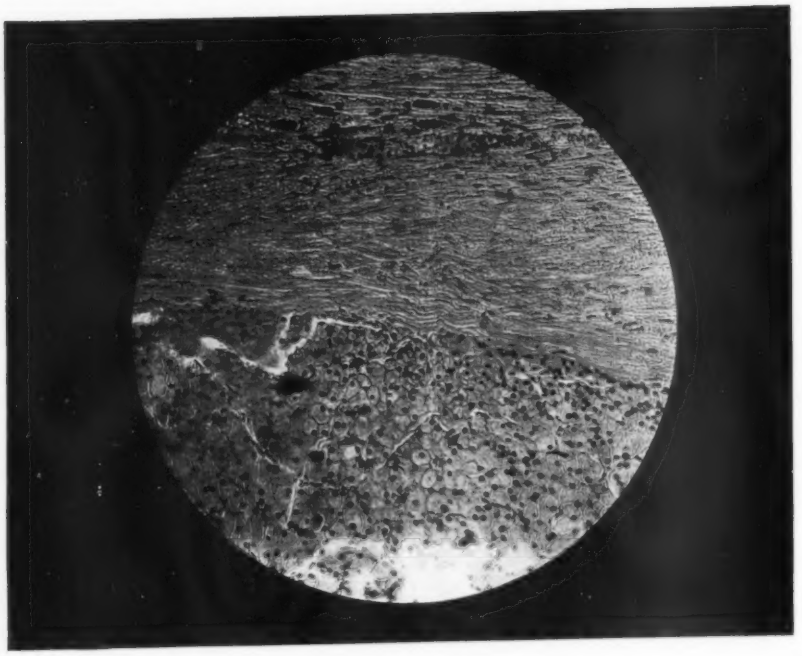
Histological Examination. The capsule of the tumor is composed of connective tissue very poor in nuclei (Fig. 2). The greater part of this tissue has undergone hyaline degeneration. Scattered here and there throughout the capsule are slit-like or round spaces lined by one layer of cuboidal epithelium. These resemble identically kidney tubules which have been compressed, and they are undoubtedly renal in nature. In a few places single or double rows of tumor cells are seen scattered throughout the connective tissue. The capsule is richly supplied with blood-vessels, the walls of which are merely composed of one layer of endothelium. The ingrowths from the capsule are also connective tissue in origin. These, however, have undergone almost complete hyaline degeneration, and in places are necrotic and infiltrated by many red blood corpuscles.

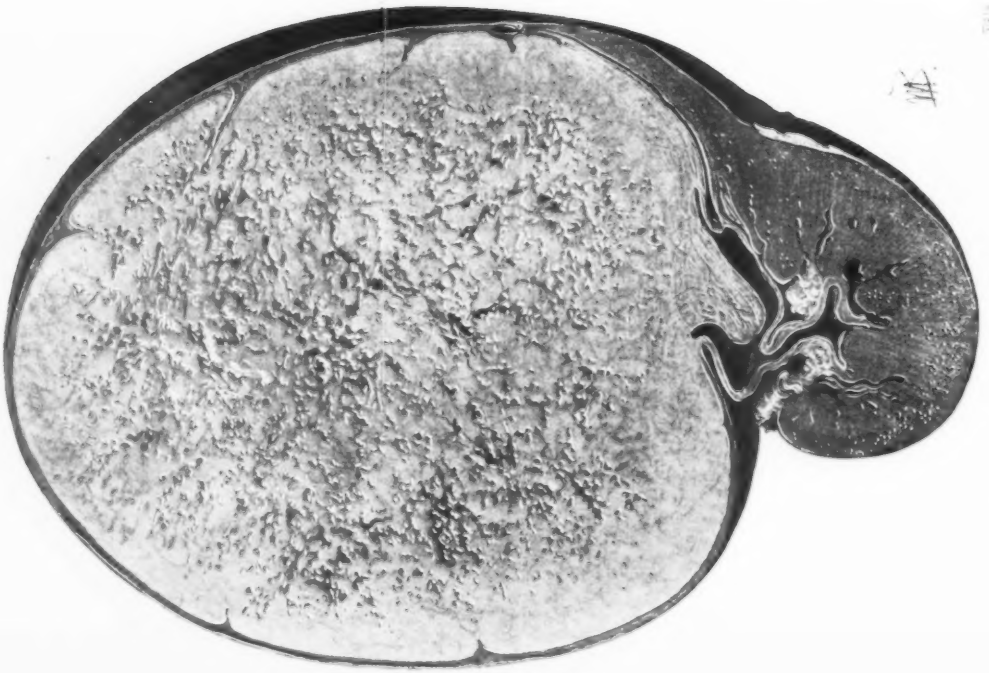
The tumor proper is made up of polygonal cells, occurring chiefly in double rows, but sometimes in rows of three or four (Fig. 2). The individual cells are sharply defined and vary considerably in size. Their protoplasm stains a light purple with hæmatoxylin, and with the oil immersion is seen to be made up of round globules, all of which are approximately the same size, and between which is a delicate granular material. The nuclei of the cells are round, elongate oval, or irregularly oval. If the cell be small they are usually situated in the centre of the protoplasm; where the cell is large they are pushed to one side. Between the double rows of cells are delicate capillaries which are separated from the cells by one layer of endothelium. Most of the capillaries are only wide enough to admit the passage of one red blood corpuscle at a time; some of them, however, are dilated. Around a few capillaries are aggregations of lymphoid cells, associated with a small amount of new-formed connective tissue. On passing inward about 1 cm. from the capsule the tumor cells are seen to be necrotic. The capillaries are somewhat more resistant and can be traced a short distance further. The entire central portion of the tumor is necrotic. Specimens were stained for glycogen, but as the tissues were hardened in Müller's fluid the results were negative.

The kidney tissue in the vicinity of the tumor is greatly altered. The glomeruli show marked increase of connective tissue cells in their capillary walls, some of them being almost obliterated. The lobules are much atrophied, their epithelium is almost flat, and their lumina are filled with hyaline casts. There is great increase of connective tissue between the tubules, and the blood-vessels are dilated. The farther away from the tumor the less the pathological change. In all parts of the kidney, however, there is considerable alteration. Sections from the lower half of the kidney, where little if any pressure was exerted, show that the glomeruli are congested and enlarged, and that between the capsule and the glomerulus is a moderate amount of granular material. The convoluted tubules are dilated, their epithelium is somewhat granular, but their nuclei are well preserved. The collecting tubules are in some places dilated, the epithelium of these being flattened and pigmented. Their lumina contain hyaline casts. Scattered throughout the kidney is a moderate amount of connective tissue, which in many places has undergone hyaline degeneration. The capillaries between the collecting tubules are dilated.

Such tumors have frequently been described under the title, "Struma suprarenalis sarcomatodes aberrans," and have been dealt with at length by Horn, a student of Grawitz, also by Lubarsch* and others. They are usually multiple, are generally found in the upper half of the kidney, and vary from a cherry to a child's head in size. Most of them are yellow or yellowish red in appearance; some, however, are grayish. Each nodule is surrounded by a fibrous capsule and appears to be sharply defined. The large tumors show areas of softening in their centres. The adrenal gland may be intact or included in the tumor. Histologically the capsules of these tumors consist of connective tissue which may contain tumor elements. The tumor is made up of polygonal cells arranged in single or double rows. Some of these cells are cylindrical, and are so arranged that on cross section they present a gland-like appearance. The cells themselves have small, round, deeply staining nuclei which are surrounded by a large quantity of protoplasm. The protoplasm contains many fat

* Lubarsch: Virchow's Archiv, Bd. CXXXV, Heft 2, S. 149.





droplets of variable size, also small droplets of a homogeneous, highly refractive substance which gives the glycogen reaction. At times giant cells are found or nuclear figures may be made out in the tumor cells. The blood capillaries are very abundant and are only separated from the tumor elements by one layer of endothelium.

Some of the polynuclear leucocytes in the vessels may contain glycogen. The central portions of the tumor are frequently necrotic, and show numerous hemorrhages. From the histological appearances some have described these tumors as carcinomata, others as sarcomata, and they have not infrequently been thought to be endotheliomata, from their vascular arrangement. Microscopically the cells of these tumors resemble almost if not identically those of the adrenal gland. Grawitz accordingly concludes that these tumors arise from the adrenal elements. It is probable that in fœtal life small portions of the adrenal gland become included in the kidney substance, and that in after-life they undergo development. Metastases are frequent, having occurred in twenty of the twenty-nine cases reported. These have been found in the inferior vena cava, having extended by continuity from the renal vein, in the capsule of the kidney, in the retro-peritoneal glands, lungs, pleura, thyroid glands, and also in the glands of the neck. The lungs and pleura are the parts most frequently invaded. The secondary growths are identical in character with the original tumor, their cells being similar in character and containing glycogenic granules. These tumors may occur at any age; the most frequent period is, however, between forty and sixty. The symptoms are indefinite. The presence of a tumor in the renal region will, however, make one suspicious. In a certain number of cases blood is present in the urine, and in one case the urine contained tumor cells.

The present case is somewhat unusual, on account of the size of the tumor, also from the fact that it consists simply of one nodule. From the histological appearances it seems certain *that the tumor originated from a portion of the adrenal gland which had been included in the kidney substance.* Whether the entire adrenal was included or not it is impossible to say. It was not found on the surface of the tumor, but may have been left in the abdominal cavity. In concluding, I wish to thank Prof. Welch for his assistance in the preparation of the pathological report, and Dr. Hoen for the excellent micro-photograph he has made.

DESCRIPTION OF PLATE.

Fig. 1. Three-fourths natural size. The upper half of the kidney is occupied by a tumor mass which is surrounded by a capsule. This capsule sends septa into the tumor substance. The outer portions of the tumor are still firm. The centre is necrotic and is breaking down. The tumor at its lower portion has grown into the pelvis of the kidney.

Fig. 2. About 250 diameters. Is a section taken from Fig. 1 at point *a*. The left half is tumor substance, the right half a portion of the capsule. In the capsule a row of tumor cells can be seen. The capsule also contains elongate-oval deeply-staining areas; these are cross sections of compressed kidney tubules.

THE BACTERIOLOGY AND PATHOLOGY OF DIPHTHERIA.*

BY SIMON FLEXNER, M. D., *Associate in Pathology, Johns Hopkins University.*

The results of the researches of Loeffler published at the close of the year 1883 may be said to mark the beginning of the new era in the study of diphtheria, and whatever doubt surrounded his first publication regarding the relation to diphtheria of the micro-organism which now bears his name, has now been finally dissipated. The isolation of the Loeffler bacillus by workers in different parts of the world from the local lesions of the disease in many thousands of cases would seem to afford irrefutable evidence of the constancy of the relationship existing between the bacillus and the pathological process. Hence it is that attention has been directed to a consideration of other aspects of the subject than that of the presence or absence of the Loeffler bacillus in primary diphtheria.

The wide divergence of opinions regarding diphtheria which existed prior to the discovery of the bacillus diphtheriæ illustrates with what difficulty every advance in the study of a disease is accompanied so long as its ætiological factor is still unknown. It had long been a well-established fact that by a variety of agents, pseudo-membranes which offered more or less the appearances seen in diphtheria could be produced upon mucous surfaces in man and in animals; but it was at the same time recognized that none of these agents could reproduce the symptom-complex of diphtheria; and none of us are likely to forget the almost interminable discussion which arose as to whether it was primarily a local or a constitutional disease. Nor did the study of its pathology give much assistance in the solution of this question, and only after the specific micro-organism had been obtained in pure culture did it become possible, by a study of its properties outside the body and of its occurrence under natural conditions in human beings, to establish a rational basis for a classification of the disease.

First of all, then, it is important to distinguish between the anatomical and the ætiological significance of the term "diphtheria," and it will be found that a limitation of the term to a disease characterized by the presence of the bacillus diphtheriæ in the affected portion of the body will do much to eliminate the confusion of pathological conditions which, while anatomically resembling one another, are otherwise quite distinct.

The first question to which I would direct your attention

* Being the substance of an address delivered on January 8, 1895, before the Alumni Association of the Jefferson Medical College, Philadelphia.

regards the proportion of cases of pseudo-membranous inflammations of the throat which are due to the Loeffler bacillus. In the first series reported by Loeffler himself, a certain number of the cases examined did not yield the diphtheritic bacillus; but of these, several were recognized as not having been cases of primary diphtheria. This failure to find the Loeffler bacillus in all pseudo-membranous inflammations in the throat and air-passages has been confirmed by later investigators. Thus in a table prepared by Escherich, in 679 examinations collected from Paris, Berlin and New York, the bacillus diphtheriæ was found in 427, or in 62 per cent. of all the cases. In a series studied by Morse of Boston, of 301 cases examined, the Loeffler bacillus was found in 217, *i. e.*, it was present in 72 per cent. of the cases. Park and Beebe report that of 5611 cases examined, positive results were obtained in 3255 (58 per cent.). The bacillus was absent in 1540 cases (27 per cent.), while 816 cases were doubtful. The doubtful cases represent those in which for some reason or another satisfactory cultures were not supplied. If these, then, be disregarded altogether—although it may not be entirely fair to do this—we find that out of 4795 cases of suspected diphtheria, 68 per cent. were instances of true diphtheria.

It is acknowledged that the pseudo-membranous anginæ which are associated with the acute exanthemata are commonly not caused by the Loeffler bacillus, but are due in most cases to the invasion of the streptococcus pyogenes. In a series of bacteriological examinations made by Booker in such cases, the bacillus diphtheriæ was constantly absent; and Escherich, who studied fourteen cases of scarlet fever, states that the Loeffler bacillus is never present in the early days of the disease, but that in several of these cases they were found to be present later on, a fact which he attributes to the imperfect separation of diphtheria and scarlet fever patients in the Munich hospital, where his studies were carried on. He also found the Loeffler bacillus in certain cases of measles and whooping-cough, and he agrees with other investigators in holding that the acute exanthematous diseases predispose to infection with the bacillus diphtheriæ.

It had been observed by the older clinicians that during epidemics of diphtheria, pseudo-membranous inflammations of the throat in the course of typhoid fever were more frequent. Morse reports four cases of typhoid fever complicated with diphtheria; at least three of which developed diphtheria after admission to the hospital.

A purely local and perhaps non-contagious inflammation of the larynx has, by the bacteriological examination of a considerable number of cases of membranous croup, been shown to occur unassociated with diphtheria. These cases, however, are quite exceptional. Of 88 cases of membranous croup studied by Martin, 59, or 67 per cent., were of diphtheritic origin. The statistics of Park indicate that in New York fully 80 per cent. of the cases of the same disease are caused by the Loeffler bacillus. Of 229 of Park's cases, in 167 no membrane or exudate was found above the larynx. Welch and Abbott, Booker, Williams, Kolisko and Paltauf, Concietti and Fraenkel have reported cases of laryngeal diphtheria in which the pseudo-membrane was confined to the larynx and lower air-passages.

It is an undoubted fact that a case of so-called membranous laryngitis has not infrequently been the first of a series of cases of genuine faucial diphtheria.

Among the most important results of the bacteriological study of the inflammations of the throat and air-passages has been the discovery that cases which present the features of a mild catarrhal angina or of a lacunar tonsillitis may be associated with the presence of the bacillus diphtheriæ, and that from these can arise other cases in which membrane is found on the fauces.

This class of cases has been studied by Escherich and Feer, and especially by Koplik. Within the past few weeks I have seen two such instances in the practice of Dr. W. D. Booker, and from them obtained the Loeffler bacilli in cultures. The first was a girl of 16 years, who came to the surgical dispensary of the Johns Hopkins Hospital for enlarged glands of the neck. Upon examination she was found to have a lacunar tonsillitis. She suffered no inconvenience other than that resulting from the swollen glands. The plugs from the crypts of the tonsils contained the Loeffler bacillus. She made a rapid recovery.

The second was a child one and a half years of age whose tonsils were greatly swollen and almost meeting in the middle line of the throat. There was no visible membrane. Cultures from the throat showed the presence of the bacillus diphtheriæ. The local treatment recommended by Loeffler was used, and by the third day all symptoms of the disease had disappeared.

Heubner has just published a short series of cases, in which he calls attention to what he describes under the title of latent diphtheria. These were secondary to other diseases than scarlet fever and measles, and occurred in the young in the course of wasting affections, such as rickets, tuberculosis, etc., in hospital practice. The symptoms were fever, gastro-intestinal disturbance, and slight bronchial and nasal catarrh. Heubner says that diphtheritic infection is not apt to be suspected in these cases until laryngeal stenosis suddenly develops, or the fact is revealed at autopsy by the finding of a false membrane in the pharynx or larynx.

Roux and Martin have found in the course of their inoculation experiments for the preparation of the anti-toxin, that animals which had been previously inoculated with other bacteria or their poisons, from which they had recovered, were more susceptible to the diphtheria toxin; and, similarly, that pregnant animals or such as had just given birth to young exhibited a similar diminution of resistance.

The mucous membrane of the nose affords a favorite resting-place for the Loeffler bacillus. In pharyngeal diphtheria these bacilli are commonly present in the nasal secretion, even in the absence of membrane in the nose. Primary diphtheria of the nasal mucous membrane sometimes occurs. Such cases have been reported by Stamm, Baginsky, Abbott, Ravenel, Czemetschka, Townsend and Park. Of the last two writers the membrane was confined to the nose in 4 and 9 cases respectively. Escherich has seen one case in which the infection of the nasal mucous membrane took place through the tear-duct in a case of diphtheritic conjunctivitis. Katz has just reported a case of faucial diphtheria which developed in

a child exposed to infection from another child suffering from fibrinous rhinitis due to the Loeffler bacillus.

Babes first cultivated the Loeffler bacillus from the pseudo-membrane in diphtheritic conjunctivitis, and reproduced the disease by the inoculation of the organism upon the conjunctivæ of rabbits. A number of cases of pseudo-membranous conjunctivitis have since been found to be associated with the bacillus diphtheriæ, although it must be stated that not all are caused by this organism. In two cases which I examined for Dr. Hiram Woods the Loeffler bacillus was not found in the exudate, but streptococci were present in both. The results of Councilman's investigations would go to show that certain cases of otitis media are due to this bacillus.

The skin surfaces of the body would appear to be immune to the action of the Loeffler bacillus in the absence of any loss of continuity. Thus Wright cultivated the diphtheria bacillus from excoriated or ulcerated surfaces of the skin in 7 cases of diphtheria; and Park found this organism in wounds of the finger received by physicians while performing intubation. Cases of wound diphtheria associated with the Loeffler bacillus are reported by Brunner, Neisser, Treitel and Abel; but it is probable that most cases of so-called wound diphtheria are caused by other micro-organisms. The relative insusceptibility of the external surfaces of the body to infection with the bacillus diphtheriæ is illustrated by the behavior of tracheotomy wounds, which only exceptionally become infected with this organism. Faltonek examined 953 tracheotomy wounds without succeeding in a single instance in isolating the Loeffler bacillus. Other observers have been more successful, but in these cases the possibility of the contamination of the wounded surfaces with the tracheal secretion cannot be excluded.

Having now passed in rapid review the situations of common localization of the Loeffler bacillus upon the surface and in the cavities of the body, I would ask your attention to its distribution within the viscera. At the time of Loeffler's first publication he expressed a belief that the bacillus diphtheriæ was to be found only at the local site of the disease, and that it did not invade the tissues at all, or at least only exceptionally. He had cultivated it, however, in one case from the lungs; and later Kolisko and Paltauf and Babes isolated in rare instances a few organisms from the internal organs. The observations of Frosch, since confirmed by others, have shown that not uncommonly a few bacilli enter the circulation and may be cultivated from the internal organs at autopsy. They are not however only small in number, but their distribution is irregular, and it is necessary to transplant considerable quantities of material in order to grow them. Frosch cultivated the bacillus from the blood of the heart, the brain, pleural and pericardial exudates, pneumonic areas in the lungs, spleen, kidneys, bronchial and cervical lymph glands and liver. Booker has also obtained the organism from the internal organs. At the autopsy of a child of three years which had both pharyngeal and laryngeal diphtheria I obtained the bacillus diphtheriæ in pure culture from the heart's blood, cervical lymph glands, liver, spleen, lungs and kidneys, but, contrary to Frosch's experience, they were present, in this case, in large numbers in the blood, glands and spleen. In this as well as in a later instance I was able to cultivate the Loeffler bacillus from broncho-pneumonic areas, and also to demonstrate them in sections from the bronchi and lung tissue. The predominating organism, however, was the micrococcus lanceolatus. Kutscher has just shown that the Loeffler bacillus exists at times in considerable numbers and may be the predominating organism in cases of broncho-pneumonia associated with diphtheria, and he inclines to the view that it is capable of causing both bronchitis and consolidation of the lung substance. Wright has found the bacillus diphtheriæ in the internal organs in cases of human diphtheria, and he has also cultivated them from the liver, spleen, heart's blood and kidneys in a small number of experimental guinea-pigs. Abbott and Ghriskey found that after inoculating cultures of diphtheria bacilli into the testicle of guinea-pigs, small nodules containing this organism sometimes appeared in the omentum; and this bacillus has also been cultivated from the ecchymotic patches in the stomach and from the surface of the membrane in croupous gastritis. Of especial interest is the case reported by Howard, in which a bacillus in all respects resembling the bacillus diphtheriæ, except that it did not possess pathogenic properties for guinea-pigs, was cultivated in large numbers from the heart-valves in a case of acute ulcerative endocarditis and from the infarctions in the spleen and kidneys.

Notwithstanding the results of later and more searching studies which have necessitated a modification of the earlier views regarding the relation of the Loeffler bacillus to diphtheria, and notwithstanding the fact that it is now known that the Loeffler bacillus can develop not only locally upon the affected mucous membrane, it must be considered as proven that only a few organisms penetrate into the body; and there are undoubted instances in which the disease has pursued a typical, severe and even fatal course in which the bacilli have remained localized in the mucous membrane. Hence the local process is still to be regarded as the chief seat of the activity of bacillus diphtheriæ.

The study of the properties of this bacillus as it exists outside the human body and the results derived from the inoculation of susceptible animals would indicate that the effects which it produces upon the body are due to a soluble poison, a toxin, proceeding from its growth and multiplication. By means of this toxin, separated from the living bacilli, all the constitutional effects of diphtheria can be induced. For the production of the false membrane the presence of the bacillus itself is necessary.

The growth and multiplication of the bacilli in the false membrane in the pharynx, larynx and nose are associated with the formation of this toxin, which, entering the body, causes the symptom-complex of the disease. Sidney Martin has extracted from the pseudo-membrane an albumose which possesses the poisonous properties of the toxin.

We owe especially to Roux and Yersin and Brieger and Fraenkel our knowledge of the nature and properties of this toxin. According to their researches it belongs to a class of substances of albuminous nature, possessing poisonous properties, for which the name tox-albumens has been proposed. Up to the present time the tox-albumen of diphtheria has not

been obtained in a pure form, but in its impure state it is found to possess extraordinary potency. Susceptible animals (rabbits, guinea-pigs, kittens) inoculated with it exhibit all the symptoms of diphtheria, not excepting the post-diphtheritic paralysis.

The study of the action of this bacillus upon animals has shown a material difference in the virulence exhibited by cultures derived from different colonies, those obtained from a single case showing at times wide variations in virulence. The guinea-pig being the animal most susceptible to its influence, is generally employed for testing these variations.

No less striking are the differences in the potency of the toxin produced by the bacillus, and it has been found that there exists a direct relation between the virulence of the organism and the intensity of the poison which it is capable of yielding.

It cannot be said that any such relation between the virulence of the organism and the severity of the symptoms has been shown to exist for human beings. Indeed, contrary to the results arrived at by Roux and Yersin—which seemed to indicate that a progressive diminution in the virulence of the bacilli corresponding with the mildness of the attack took place, and that the same thing happened during convalescence from a severe attack—Escherich, Tobiesen, and especially Wright, have shown that no such diminution of virulence occurs. Fully as virulent organisms may be found in cases which are mild from a clinical standpoint as in those of severer grade.

The question of individual predisposition or of resistance to the invasion of the bacillus diphtheriæ and to the effects of its toxic products has therefore to be considered in this as in the case of other infectious diseases. What the physical basis for this distinction really is we are probably still far from having discovered. A few of the conditions which favor or inhibit infection in human beings and in animals seem clear. Hence it is that the results of the recent studies of Wasserman and Abel upon the action of the blood-serum of healthy human beings upon animals previously inoculated with the Loeffler bacillus are suggestive, as they indicate that the serum of certain individuals contains some protecting substance, the power possessed by the serum of adults being greater than that of children.

It is quite established that the bacillus diphtheriæ may possess all grades of virulence down to complete absence of pathogenic power, and some confusion has arisen by the introduction of the term "pseudo-diphtheritic" bacillus to denominate an organism which, while it resembles the true bacillus diphtheriæ, is devoid of virulence for guinea-pigs. This bacillus was first isolated by Hoffmann, who regarded it as identical with Loeffler's bacillus. Roux and Yersin advanced the view that this so-called "pseudo-diphtheritic" bacillus represents an attenuated form of the true bacillus diphtheriæ, and the work of Abbott, Park, Koplik and Escherich lends support to this position. On the other hand, it is suggested that the name "pseudo-diphtheritic" should be reserved to designate bacilli which, though resembling the true diphtheritic bacillus, show certain cultural differences and are devoid of pathogenic effect for guinea-pigs. Such a pseudo-diphtheritic bacillus has been found in a few cases of genuine diphtheria associated with the true bacillus diphtheriæ.

It must be confessed that our knowledge of the relation of the Loeffler bacillus to diphtheria and associated pathological processes has been much extended in the past few years. Thus this organism has been found in a large proportion of all cases of pseudo-membranous inflammation of the throat, and is the probable causative agent in all cases of true diphtheria. Those pseudo-membranous anginæ in which the Loeffler bacillus is not found are characterized in themselves and distinguished from cases of true diphtheria by the mildness of their course, their slightly contagious character and their low mortality; in Park statistics, excluding those associated with scarlet fever, the death-rate was 1.7 per cent.

That virulent diphtheria bacilli may be present upon the mucous membrane of the pharynx without giving rise to a false membrane is proven by those cases of pure laryngeal diphtheria from which the bacilli have been cultivated from the pharynx. Loeffler found in the throat of a healthy child a bacillus which was identical with the true bacillus diphtheriæ; later Hoffmann, Fraenkel and Feer found it under similar circumstances. In 330 healthy persons examined by Park and Beebe, who gave no history of contact with diphtheria, they found the non-virulent organisms in 24, virulent bacilli in 8, and pseudo-diphtheritic bacilli in 27. The examinations included for the most part children. Of the 8 cases in which virulent bacilli were found 5 were children in an asylum where from time to time true diphtheria occurred. Of the remaining three, one was from a house where a supposed case of croup had existed three weeks before. Two of the 8 children developed diphtheria some days later; the other six remained healthy. Loeffler recently examined the throats of 60 school children and found diphtheria bacilli in four. Of these two subsequently developed diphtheria, one a slight inflammation of the throat, the fourth remaining well.

The study by Park of the throats of persons exposed to diphtheria has shown that in 50 per cent. virulent Loeffler's bacilli are present. Of these 40 per cent. developed later the lesions of the disease. Park states that in the families from which his statistics covering this point were obtained the conditions for the transmission of the disease were most favorable. On the other hand, in families where the patient suffering from diphtheria had been well isolated, the bacilli were found in less than 10 per cent. of the healthy children.

Considered in the light of our present knowledge of the common existence of pathogenic micro-organisms, such as streptococci, staphylococci and pneumococci, in the mouths of healthy persons without necessarily doing harm there, these facts of the occasional occurrence of virulent diphtheria bacilli in the throats of healthy persons are less surprising. Doubtless it is necessary that a certain susceptibility to their action—a predisposition, if you prefer, must exist before their peculiar effects can be exerted. I beg to recall in this place the experimental results obtained from healthy human blood-serum as bearing upon this point. However, the figures furnished by Park and Loeffler would indicate that the presence of the bacillus diphtheriæ in the throat is far more significant even for the individual himself, to leave out of

consideration for a moment those with whom he may come in contact, than are the other pathogenic organisms mentioned.

The bacteriological study of convalescent cases shows that virulent bacilli may persist for a time after the disappearance of the false membrane. They are not uncommonly present after 2 to 3 weeks, and in a few instances they have been found after a much longer period. In a case reported by Park, and one also by Abel, they were still demonstrable on the 56th and 65th day respectively after the membrane had entirely gone.

The severity of the case has no influence upon the duration of the presence of the bacilli; the occurrence of nasal diphtheria as a complication seems to favor this persistence. Tezenas found in 12 cases complicated with nasal diphtheria that for a long time after the membrane had disappeared a serous exudation from the nose continued. In ten of these cases Loeffler bacilli were demonstrable so long as the secretion persisted, although they had long ceased to be present in the throat. Hence where cultures cannot be made it is recommended to continue the isolation of the patients for at least three weeks after the disappearance of the membrane.

It is probable that the bacillus diphtheriæ is capable of increasing only within the body of infected persons or in the seat of inoculation of susceptible animals. The bacilli are, however, able to remain alive and in a condition capable of causing infection for a considerable time when outside the body. Conditions which promote the drying of the organism and exposure to strong light are unfavorable for the preservation of its vitality. The individual Loeffler bacilli quickly die when allowed to become air dry. But in bits of mucus or membrane, particularly if protected from the light and preserved in a damp place, they may remain alive for a long time—upon old cultures from 5 to 15 months; in bits of membrane from 4 to 17 weeks. They have been cultivated from tableware and toys; from soiled linen which had been in contact with the sick; from the shoes and hair of nurses, and from the broom used to sweep the floor of a diphtheria ward. In view of these facts it is unnecessary to point out the importance of thorough disinfection and of the rigorous care that should be observed in disposing of the excreta of the sick.

The association of other micro-organisms with the bacillus diphtheriæ in the false membrane is by no means uncommon, although cases of pure diphtheritic pseudo-membranous inflammations are said to exist. The organisms usually associated with the Loeffler bacillus are the pyogenic cocci, strepto-, staphylo- and diplococci. Their presence is now known to be of great clinical and pathological significance, especially if they enter the deeper tissues, as they are wont to do. While the bacillus diphtheriæ is found only exceptionally in the adjacent lymph glands and internal organs, there exists a group of cases of poly-infection, especially with streptococci, in which the latter enter the circulation and invade the organs. Since the introduction of the anti-toxin treatment of diphtheria this class of cases has attracted especial attention. These cases had been recognized and studied by a number of investigators, and in this country especially by Councilman and his associates. Broncho-pneumonias, suppurations of lymph glands and septic forms of diphtheria are attributed to these associated bacteria, particularly to the streptococcus. Roux and Yersin first pointed out the importance of this poly-infection, and subsequently Schreider, Mya, Barbier and Martin confirmed their observations. Funk, Roux and Martin and Bernheim have recently made careful experimental studies on this subject. The latter employed only organisms which had been associated in the diphtheritic membrane, and he found that the virulence of the Loeffler bacillus is increased both by being grown with the streptococcus or in the filtrate obtained from streptococcus cultures. A limited number of experiments with staphylococci did not show a similar increase in the virulence of the bacillus diphtheriæ, a result confirmatory of Mya's earlier experiments. On the other hand, in human beings, according to Morse's statistics, cases of poly-infection with staphylococci run a more unfavorable course than those with streptococci. Welch has criticized his conclusions and shown the improbability of their correctness.

The natural variation in virulence of the bacillus diphtheriæ led first unintentionally, and later purposely, to the rendering of animals immune to subsequent inoculation to the Loeffler bacillus. But it was soon observed that this method of securing immunity was capricious and unreliable. The use of cultures of bacilli attenuated by chemical agents, the injection of tissue fluids into another of an animal dead of a previous inoculation of the bacilli, the employment of sterilized bouillon cultures and of cultures grown in infusions of cellular organs, such as the thymus gland, while attended with success in some cases, were found to be precarious methods of securing immunity, and not at all adapted to large animals. The use of a virus obtained from bouillon cultures several weeks old by filtration has been successfully employed by Behring, Ehrlich and Wasserman, Roux and others, to render even large animals such as the horse immune to large doses of diphtheria cultures. And one of the surprising and significant facts which has resulted from the study of the changes induced in the body fluids of the immune animal consists in the discovery that they contain a substance which is capable of rendering other animals, and even human beings, immune from diphtheria and also of curing the disease after its development.

This anti-toxin obtained from the blood of immune animals, though antidotal to the poison of the bacillus diphtheriæ, exerts no power over the poison produced by the bacteria associated with the Loeffler bacillus in the pseudo-membrane, and thus it becomes clear why cases of poly-infection are less influenced by the anti-toxin treatment than those of pure diphtheria.

It is but a confirmation of an intuitive belief to find that in the blood of human beings well of diphtheria there exists a body similar to that found in immune animals. The experiments of Klemenciwicz and Escherich proved the correctness of this supposition, and Abel has just furnished a large series of observations with confirmatory results. In animals a certain time elapses after the inoculation of the toxin before the anti-toxin appears, and it is only after repeated doses at intervals that a high grade of anti-toxic power is developed in the blood-serum. In human beings the blood taken on the 5th or 6th

day after infection shows no protective action; the protecting power appears from the 8th to the 11th day, and it persists a variable time. Sometimes it fails to appear at all. After some months it may be still present, though in a diminished degree, or it may have entirely disappeared. The longest periods of its persistence yet observed are 150 and 200 days.

These facts bear out the experience of physicians who have noted that diphtheria is not one of those diseases one attack of which affords protection to subsequent infection. Perhaps the individual differences observed are to be explained by the variation in the amount of healing and protecting substances formed in any case.

In cases of genuine diphtheria the Loeffler bacilli are found in large numbers in the pseudo-membrane, there being less in the deeper than in the older and more superficial parts. A lesion of the surface provides a condition favorable to their settlement and increase, a fact also borne out by experiments on susceptible animals. Where no previous defect exists it is probable that the toxin itself can cause a superficial lesion. The tonsils, which are the starting-points of many cases of diphtheria, afford an excellent nidus for the bacilli, on account of the incompleteness of their epithelial covering, even in health. The depth and extent of the necrosis of the mucous membrane vary in different cases; and the character of the pseudo-membrane is affected by the nature of the underlying structures; in the pharynx it is firmer and less easily separable than in the larynx and trachea, where a distinct basement membrane is found in the mucosa.

The earlier workers in the field of experimental diphtheria failed to find in the internal organs the lesions which had been described by Oertel in the tissues of human beings dead of diphtheria. These lesions consist of foci of cell-death characterized by extensive destruction and fragmentation of cell nuclei. In such areas of necrosis fibrin may be deposited. Dr. Welch and I confirmed and extended these results of Oertel by experiments upon guinea-pigs, kittens and rabbits. Subcutaneous inoculation of cultures of the organism or of the filtrate in a bouillon culture 4 or 5 weeks old, produces, besides the local lesion peculiar to each, foci of cell-death in the adjacent lymph glands and in the lymph glands throughout the body; in the spleen, liver, lungs, heart muscle and intestinal mucosa. The kidneys show degenerative changes. When the dose is small and the animal lives several weeks the paralysis which belongs to the disease may develop. This phenomenon, first observed in animals by Roux and Yersin, was noticed among our animals. Interesting changes have been described in the peripheral nerves under these conditions by Sidney Martin. In some cases he observed defects in the myeline sheaths, which stained poorly in osmic acid, while in certain severe cases the sheaths had entirely disappeared. The axis cylinders were either intact or had undergone granular degeneration, and the continuity of some of the fibres had become broken. At times the muscles supplied by these nerves showed signs of fatty degeneration. These changes agree with those found by Gombault, Meyer, Leyden and Arnheim in human beings who had suffered from diphtheritic paralysis.

Albuminuria is a not infrequent complication of the disease, and casts may appear in the urine. In some cases the urine may be much diminished in amount, but uræmia is unusual; and hydrops, which seldom occurs, is, when present, of a mild grade. The heart is not uncommonly involved, and the lesions described are either parenchymatous degeneration, in the severer grades, associated with fatty degeneration, or interstitial myocarditis. The lymphatic glands of the neck become swollen, but show a slight tendency only to suppuration. Various complications due to the invasion of secondary micro-organisms occur.

A CASE OF CHOREA MINOR OCCURRING DURING AN ATTACK OF MANIACAL EXCITEMENT IN AN ADULT.

By Henry J. Berkley, M. D.

[*Read before the Johns Hopkins Medical Society.*]

Mary H., æt. 47 years, was admitted to the City Insane Asylum on August 27, 1894, with subacute mania and general chorea, the musculation affecting the entire body.

The maniacal attack, which was preceded by a prodromal period of several weeks, began about the middle of July, and according to the report of the physician in attendance, was unaccompanied by fever, but, on the other hand, the circulation was very defective, the extremities being cold and bluish. In the third week after the beginning of the mental excitement slight jactitations of the facial and arm muscles were noticed. These muscular movements increased in severity, until the chorea was as severe as an ordinary case of St. Vitus dance in childhood.

On admission the patient was considerably excited, incoherent, talked in a rambling, silly manner, and had general choreic movements that were especially well marked in the upper extremities and in the facial muscles. There were, however, movements of almost all the other muscles. The hands and arms were moved in an irregular, purposeless way, the time of the contractions not differing in any manner from an ordinary case of chorea minor. There was no tremor about the facial or small muscles of the hands. The gait did not betray any incoördination, but the finer tests could not be applied on account of the mental condition. Articulation was not interfered with.

The physical examination showed a very anæmic woman, without bodily deformity or visceral disease. The heart's action was weak, rapid, ninety-six beats to the minute, but

there was no murmur. There was no elevation of temperature. The tongue was furred, the vegetative functions disordered. Menstruation had entirely ceased for several years.

The irides were slow to react to light or accommodation. The deep reflexes were subnormal, the superficial a little slow. The urine contained neither sugar nor albumen.

During the month of September the choreic movements gradually diminished in intensity, though no medicine was given to influence them, and by the middle of October had almost ceased, only an occasional incoördinate movement of the facial, arm or neck muscles betraying the presence of clonic spasm.

On October 17, the patient was again thoroughly examined. The mental excitement had almost abated, and the woman was considerably demented. She would occasionally answer a direct question by some irrelevant monosyllable, usually the word "why" to all interrogations. The physical condition had improved considerably, the eye irregularities and the deep reflexes had returned to the normal. There was no heart lesion, both the first and second sounds being clear. The pulse was rapid, ninety-six to the minute, there was no irregularity.

December 28.—The physical condition of the patient is still improving, while the mental remains stationary or is slightly worse. The mental reduction is very considerable; she is untidy, tears her clothes and soils her room. Will occasionally answer a question, though never to the point. The pulse now stands at one hundred and four beats a minute. The irregular muscular movements have entirely ceased for a number of weeks, having endured in all a little more than three months.

The family history offers but a single point of interest, namely, that two of the woman's three children (both girls) had chorea in childhood, from which they made a perfect recovery. The third child, a son, is not bright, and the whole family seem to be below the average in intelligence.

The family deny that there have been cases of insanity among its members, also, positively, that the mother ever had a previous attack of either chorea or insanity, a statement that is corroborated by an elder sister of the patient. On the other hand, they state that she has always been healthy until the past June, at which date the first symptoms of the mental disorder were noticed.

The family are in poor circumstances, and it is more than probable that insufficient and improper food played a large part in the causation of the mental trouble.

Whether the chorea had as its genesis an infection beginning during the first weeks of the maniacal excitement is problematical; certainly there was no coexisting rheumatism or other febrile disease at the time.

The case reverses many of our accepted ideas of the mental condition in chorea minor, and in this respect appears to be unique. Occasionally in chorea we find pronounced disturbances of the faculties of memory and attention, as well as other important mental faculties, and rarely acute melancholia may be present, or the patient may become in some degree demented, but in all forms of chorea, including chorea insaniens, the choreic movements always precede the mental disturbance, and never follow in its course. Again, primary chorea in a woman of forty-seven years running the course of an ordinary attack of St. Vitus dance, and tending eventually to a full recovery in the course of twelve to fourteen weeks, is practically unknown; such cases as do occur in this decade of life ordinarily inclining toward a chronic progressive type, and are not properly to be classed among the Sydenham choreas.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Meeting of January 21, 1895.

DR. ABEL in the Chair.

Progressive Neural Muscular Atrophy.—DR. H. M. THOMAS.

The two cases which I bring before you to-night illustrate a very interesting and rare form of muscular atrophy. One of the patients is at present in the hospital, and the other, his sister, kindly comes, so that we can have the opportunity of seeing them together. They both complain of weakness in the feet and hands, and besides this, as you see, the brother is suffering from another troublesome affection.

The family history of these cases is of interest. The brother says that their father's uncle on his mother's side and the son of this uncle also suffered with trouble in the hands and had difficulty in walking. Another first cousin of the patient's father, his mother's sister's child, also suffered from what was thought to be the same trouble. As far as they know, the patients here now are the only members of the family affected in the present generation.

The history of the patient is as follows: E. H., æt. 36, Dispensary No. 86,927, applied to the dispensary for relief from the spasmodic movements about the neck and face. So far as he knows he was well as a young child and learned to walk at the proper time. He thinks that he was able to play as well as other children, but remembers that he never could learn to skate. When he was eleven years old he had some sort of skin affection of the chest for which he was salivated, and to this date he ascribes the beginning of the trouble in his legs. He was at that time unable to walk for a week. He had scarlet fever when he was about thirteen years old, followed immediately by typhoid fever, after which he had dropsy. Following this illness he had some difficulty in speaking plainly, which has gradually become worse. At first the weakness in his legs gave him very little trouble and he was inconvenienced only when he ran. He taught school from the time he was seventeen until he was twenty-one, when he had to give it up on account of his difficulty in speaking. When he was about nineteen the weakness in his ankles had progressed so far that they would turn under him and cause him a great deal of pain. After giving up his school he learned to telegraph and was employed in this occupation up

to three years ago; although he never was a rapid operator nor did he write a very good hand He himself noticed nothing particularly wrong with his hands until his attention was called to them here in the hospital. The weakness in his legs increased very gradually, and the deformity which is now present developed equally slowly. He has never complained of any sensory symptoms.

The spasmodic movements about his head and neck are difficult to bring into relation with the muscular atrophy, and perhaps it would be better to consider them as a separate affection. They began ten or twelve years ago, when he was about twenty-five years old. At that time he noticed a slight twitching in the muscles of the right side of the neck, coming on every afternoon and lasting about an hour. The twitching at first was slight and did not cause any movement of the head; it gradually increased and became more constant, until after a time he was never free from it, and the muscular contraction became so great as to cause movements of the head. At first he had some slight voluntary control of these movements. He was operated on twice in Chicago, the nerve having been once stretched and once cut. He derived no benefit from these operations and the disease gradually involved other muscles, spreading to the other side of the neck, and four or five years ago to the muscles of the face. At times he has slight tremors of the muscles of his arms and hands. Any excitement increases the movements; they, however, entirely cease during sleep.

As you see, the patient's head is usually held bent towards the left shoulder, with the chin up, and is in constant motion, the chin often being depressed and twisted until it touches the left shoulder. Occasionally the head is turned to the right. From time to time the muscles of the face are all thrown into tetanic contraction. Any effort to speak exaggerates these facial contortions. The platysmæ also are involved in the spasm. Every now and then the contractions cause slight movements of the shoulders and arms.

The patient speaks in a peculiar muffled voice, and often seems compelled to make a great effort to overcome some spasm of the muscles of articulation. Some words are, however, brought out in a clear, distinct tone.

We are inclined to think that this distressing spasmodic affection of the muscles is an example of torticollis involving many more muscles than is usual. This is in itself a most interesting condition, but this evening I wish to call particular attention to the case in respect to the muscular atrophy. You will notice that both feet are deformed, the left rather more than the right, but both in the same manner (Fig. 1). The heels are somewhat drawn up, the soles of the feet are opposed, the arches of the feet are exaggerated, and the feet are very thick through the instep. The toes are dorsally flexed. On the outer edge of each foot there are large hard calluses, due to the position of the feet in walking. There is very little evident atrophy about the legs or feet. The thighs, fifteen cm. above the patellæ, measure fifty-three cm. The largest circumference of the calves is thirty-four cm. All the muscles moving the hip-joints and the knee-joints are very strong. In flexing the ankles, the tibialis anticus seems to be the only muscle acting. An endeavor to make passive extension brings about exaggeration of the deformity. The peronei seem to be completely paralysed. The extensors are strong. The movements of the toes are very limited, but they can still be moved feebly.

No disturbance of sensation could be demonstrated. The knee-jerks and the reflexes from the Achilles tendons are abolished. The skin reflexes, plantar, cremasteric and abdominal, are active. In the calf muscles on both sides can be noticed wave-like muscular contractions, which are somewhat coarser than what are usually called fibrillary contractions.

The patient walks with a clumsy shuffling gait on the outer edge of the feet with the toes turned in.

If you examine the arms you will notice that the muscles of the neck and shoulder, arms and fore-arms are well developed, but that there is a marked atrophy in the small muscles of the hands. This is especially evident in the space between the thumbs and forefingers (Fig. 2), and on the ball of the thumbs. The muscles about the shoulders and elbows are strong, and also the muscles moving the wrist show no marked weakness. Adduction and abduction of the fingers are very weak, as are also the movements of the thumb. No fibrillary contractions are noticed in the arms; no reflexes are obtained from the tendons of the triceps muscles, and we have been unable to demonstrate any change in sense perception.

The electrical examination in the muscles of the arms and legs revealed a remarkable condition. The small muscles of the hands could not be made to respond to either the faradic or galvanic currents, nor could I, with any strength of current that the patient could stand, cause a contraction in any of the flexor muscles of the ankles except the tibialis anticus muscles. And in general the nerves and muscles of the arms and legs responded, if at all, only to extremely strong currents; thus—the ulnar nerve above the elbow showed a slight K. Cl. C. to a current of 8 M. A.; the musculo-spiral to 10 M. A. During the examination it was noticed that the muscles of the fore-arm were the seat of slight irregular spasmodic contractions. The muscles of the arms and legs in general responded normally to mechanical irritation.

The history of the sister is as follows:

Mrs. R., æt. 28, Dispensary No. 87,679, thinks she was a strong little girl, had measles, but can remember no other illness. Has been married eight years; has never been pregnant.

When about twelve years old her feet began to get a little weak, although at this time she paid very little attention to them. At times her ankles would turn under her and she was unable to learn to dance, or to take part in games that required much running. Her ankles gradually became weaker, and when she was eighteen years old she was advised to put on braces; this she did, and wore them for three years, but finding that they did not help her she discontinued their use. Her feet have very slowly grown worse, the right foot being worse than the left, and she has noticed that she has very little power over the right great-toe.

For the last five or six months the patient has had numb and tingling sensations in her hands, and when they get in the least cold she is unable to perform any of the finer movements with them, such as getting coins out of her purse, or a key out of her pocket and unlocking the door. She has not

FIG. 1.

FIG. 2.

noticed any other weakness about her hands nor any atrophy. She has occasional twitchings about the eyelids, but no other jerkings in the muscles.

Her general health is good.

Upon examination I think it is evident that her legs below the knee are smaller than they should be; she flexes the ankles fairly well, but in resisting my efforts to extend them, the toes are turned in, the inner border of the foot is drawn up, and the foot assumes a position quite similar to that of her brother's. The tibialis anticus is the only muscle of this group that is at all strong, and in short the same muscles are involved as in her brother, although in a less degree. The knee-jerks are present, but are somewhat subnormal.

In her hands, as you see, there is undoubtedly beginning atrophy of the small muscles, and their resemblance to her brother's is evident.

No fibrillary contractions have been noticed anywhere, and we have been unable to demonstrate any sensory changes.

The electrical examination revealed the same condition as that described in the case of her brother, and it is quite startling to apply very strong currents to muscles which act well voluntarily and receive no response.

I think there can be no doubt that these patients are suffering from the same disease, and it seems probable, although of course not certain, that the other members of the family mentioned in the history were similarly affected.

We have here a disease occurring in a family, characterized by a slowly progressing weakness and atrophy of certain muscles, beginning at about the time of puberty, in the muscles of the legs and feet, especially the peroneal group; accompanying this weakness there has slowly developed a deformity of the feet, *equino-varus;* years after the onset, the small muscles of the hands have become involved, so slowly that it was not noticed by either patient.

Associated with this change in the muscles there is a very remarkable electrical condition. The muscles most involved cannot be made to contract by any current that can be used. In most of the other nerves and muscles of the body there is a very great decrease in their electrical excitability.

So far the symptoms are parallel in the two cases, but the sister complains of distinct subjective sensory disturbances, from which the brother is apparently entirely free. No fibrillary contractions or similar phenomena were detected in the sister's muscles, whereas in the muscles of the brother's calves there are coarse fibrillary contractions, and a peculiar unrest in the muscles of the fore-arm, not to speak of the intense torticollis, which is his most distressing complaint, but which we are at present unable to associate with the disease under discussion. It is, however, quite possible that a more extended examination of the sister might reveal some fibrillary contraction. In the brother the deep reflexes are abolished, and although present in the sister, are distinctly less active than is usual.

These cases are good examples of that form of progressive muscular atrophy which seems to occupy an intermediary position between the *spinal* forms on one side and the group collected together under the name of *muscular dystrophies* on the other. It is known by several names, and there is still a good deal of discussion about its pathology. Cases belonging to this class were described as early as 1856 by Eulenburg. Eichorst also described similar cases in 1873, and Osler in 1880 described a most interesting family, the Farr family of Vermont, in which many members were affected by an unusual form of muscular atrophy. Hammond in 1881, Ormerod in 1884, and Schultze in 1884 each recorded cases. Charcot and Marie (Revue de Médecine, 1886, p. 96) collected a number of cases, recognized them as a peculiar form of muscular atrophy and gave a very clear clinical picture, so that this form of muscular atrophy is known in France as the Charcot-Marie type.

Tooth (Brain, 1887), in England, quite independently describes the disease under the name of *muscular atrophy of the peroneal type.* He was followed by Herringham (Brain, 1888). Hoffman (Arch. f. Psych. etc., 1889, p. 660), in a long and thorough article, reviews the subject and suggests the name progressive neurotic muscular atrophy, as indicating his belief that the pathological basis for the disease was a slowly progressive degeneration of the peripheral nerves. Sachs of New York (Brain, 1890) wrote of the disease as the *peroneal form* or *leg type* of progressive muscular atrophy. He considered it a form of the *spinal* atrophies beginning in the legs. Hoffman's second article appeared in the first volume of the Deut. Zeitschrift f. Nervenheilkunde, in which he thinks it better to call the disease progressive *neural*, instead of *neurotic*, muscular atrophy. Bernhardt (Virchow's Arch., Bd. 133, 1893) proposes as a name for the trouble *progressive spinal neuritic muscular atrophy*, as he thinks that the spinal cord as well as the peripheral nerves are involved. Ferrier is of the same opinion (Brit. Med. Jour., 1893) and he suggests the name *myelo-neuropathic amyotrophy.*

The authors agree well as regards the clinical picture. It occurs either as a hereditary or a family affection. It often begins in childhood, causing great deformity of the feet. The muscles first affected are usually the small muscles of the feet and the peroneal group. The progress is very slow, and usually after several years the small muscles of the hands become affected before the muscles of the thigh show any weakness. In fact in certain cases the disease may begin in the hands (Hoffman). The disease may not begin until puberty or adult life. It is often accompanied by both subjective and objective sensory disturbances. The deep reflexes may be normal, diminished, or abolished. Fibrillary contractions and muscular twitchings are often present. Very generally there are marked changes in the electrical excitability of the nerves and muscles, consisting either in a loss or a very great decrease of the excitability, and this can often be demonstrated not only in the atrophic muscles, but also in nerves and muscles that are performing their functions quite normally. Bernhardt has described the case of a member of a family in which this disease occurred, who only complained of becoming tired very easily and in whom he demonstrated this remarkable electrical condition and was from this able to make the diagnosis.

In regard to the pathology, not a great deal is known. Hoffman refers to two old cases, one by Virchow and one by Friedreich, in which was found a marked degeneration in the

peripheral nerves as well as some slight degeneration in the columns of Gall, and he refers to the record of a case by Dubreuilh (Rev. de Méd., 1890) in which was found old degeneration of the nerves, most intense at the periphery, decreasing towards the spinal cord, and just observable in the anterior cervical and lumbar roots. There was also a slight increase of the neuroglia of the columns of Gall, and the pyramidal fibres were somewhat more deeply colored than usual. The gray matter of the spinal cord was normal. There were well marked degenerations in the muscles.

Hoffman does not consider that these observations determine whether the disease is primarily in the spinal cord or the peripheral nerves, but thinks that especial emphasis should be laid upon the lesions of the nerves as distinguishing these cases from the ordinary spinal form of progressive muscular atrophy, and I think we cannot go far wrong in following him in calling these cases *progressive neural muscular atrophy.*

Dr. Osler.—This disease is of great interest on account of its rarity. There have been very few observed in this country; I think Dr. Sachs has reported the only one. The Farr family, which came under my observation some years ago, had 13 members affected in two generations. I had a letter the other day from the son of my old patient, Wesley Farr, and he states that none of the members of his generation or in his family or in his cousins' have been affected. Many of them now are men and women past the adult period. He mentions that if the disease is beginning in him at all it is beginning with a "yanking" in his eyelids. It is rather remarkable in that group that in all the members affected it began late in life, all over 40, which has raised some doubt as to whether that family actually belongs to this type of the progressive muscular atrophies. These are the only cases we have ever had at this hospital.

Meeting of February 4, 1895.

Green Hair.—Dr. Oppenheimer.

Dr. Oppenheimer presented a specimen of green hair. The hair was from a patient, aged 58, a coppersmith, who came to the medical Dispensary in July, 1891. He had been a workman in copper works for four years, exposed to very fine copper oxide dust. He was not very cleanly in his habits. Since half a year or so he had had vague stomach symptoms; nausea, occasional vomiting, some distress, but no actual pain after eating; no colic. No pulmonary symptoms were complained of, and the examination of the chest and abdomen was negative. There was no line on the gums. He did not return after the first visit, but it was ascertained that he died two years later with a severe cough.

The chief point of interest was the hair. Like the specimen presented, it was a pale but quite distinct green. This was more true of the hair on the head and of the moustaches, but all over the body, in the axillæ, over the pubes and shins there was the same coloration. Copper was easily demonstrated chemically. Microscopically the hair was uniformly colored, no crystals being seen anywhere. The color was less marked towards the root of the hair. Boiling in water did not remove the color, but ammonia did so at once.

Greenish hair with men in copper works and in copper mines is not unknown. As far back as 1654 Bartholin noted its occurrence. Several observers since then have remarked on it, Kobert, in his "Intoxications Krankheiten," and Hirt, in his "Krankheiten der Arbeiter," both mentioning it. Petri in 1881 reported a case in which the root of the hair was free and crystals were to be seen.

On questioning at the copper works, it was found that the patient was an exception, the majority of men being free. They state, however, that it is only by scrupulous cleanliness that they avoid the coloration. They must wash their hair daily in a solution of soda, as ordinary water is ineffectual. The part first apt to be affected is the moustache, and next the head; though, if the latter is protected by a thick cap, it will be free. The color appears a few days after starting work, and is more apt to come in summer time, when they sweat freely. Then the underwear has a greenish tinge, wherever it has been thoroughly wet with sweat. They seldom have any gastro-intestinal disturbance, but a severe, distressing cough is not uncommon, and occasionally ends fatally.

Brassfounder's Ague.—Dr. Oppenheimer.

Dr. Oppenheimer also presented a case of "Brassfounder's ague." The patient came into Dr. Osler's wards first on October 9, 1894, complaining of colic and general weakness. He had been a workman in a large bell-foundry in the city for 4 years, employed in a room where the metal is melted. He was regarded as a case of lead poisoning; the colic, extensor weakness and a blue line on the gums pointed to this. He had also mitral stenosis. He left the wards October 15, 1894, and was again admitted on January 18, 1895, for dyspnœa, and other symptoms, due to lack of compensation. He gave the following history as regards his chills:

He is employed in the room where the metal is melted. For this, old copper, zinc and brass are melted in a vat; white fumes arise, and are inhaled, giving rise to a feeling of fulness and distress in the chest, and coughing. Later new copper is added, but this does not give rise to any fumes. He begins work at 7 A. M., and all melting is over by 4 P. M. If he is to have a chill, when he gets into the open air he feels tired and has pains all over, especially in the joints. About 6–7 P. M. he has a severe shake, lasting 1–2 hours; he takes a whiskey punch, goes to bed and sweats profusely; then he falls asleep. The next morning he feels exhausted and tired, enough so at times to keep him from work.

The following circumstances increase the probability of a chill:

1. Absence from work for some time previous.
2. Damp, cloudy weather.
3. Poor ventilation; thus the chills are more frequent in winter than in summer.

Out of 28 workers in his department, all have had chills. On a bad day nearly all will have a paroxysm. There are seldom less than two or three laid off, and occasionally all have been absent. There seems to be no difference in susceptibility.

According to Hirt, these chills were first called attention to in 1844 by Blaudet. Greenhow reported several cases in

1862, and his conclusions were practically the same as the patient's. Hirt had two paroxysms after inhaling the fumes. His description is as follows: "A few hours after inhaling the fumes there is a peculiar, uneasy sensation through the whole body, a feeling of prostration and weakness. This is combined with drawing pains in the back, and soon one is obliged to stop his work. Muscular pains appear next, at times in the upper, usually in the lower limbs; these may become very intense. With all this the pulse is quiet and the respiration not hurried. Soon after going to bed a general shivering appears, which usually increases to a well defined chill, lasting fifteen to twenty minutes. The pulse becomes rapid, as high as 120 to the minute. Coughing, which at first is unimportant, not more than a mere tickling in the throat, becomes severe and distressing, giving rise to soreness in the chest. Frontal headache sets in and is intensified with each paroxysm of coughing, making the condition almost unbearable. However, the height of the paroxysm is soon reached (in three to six hours), and the stadium decrementi begins with a profuse sweat. The symptoms abate and the patient falls into a deep sleep, from which he awakes with a quiet pulse and respiration, no cough, and only a slight headache, and some weakness to remind him of the paroxysm."

The description tallies very well with the patient's except that the after-effects were severer with the patient.

The white fumes, arising from the vats, precipitate as a powder. Dr. Aldrich has kindly examined this, and finds it contains zinc oxide and carbonate, but no arsenic.

Exhibition of Surgical Cases.—DR. PLATT.

Case 1. This boy, 11 years of age, came to us some seven weeks ago. He was run over by a heavy express wagon and fractured his right thigh. He was neglected by his parents or physician, or all together, for 15 days, and when he entered the Garrett Hospital the thigh was bent at a right angle at the point of fracture. I bring him before you to show what an excellent result can be gotten in a boy; a much better result than could be obtained in an adult. The injured extremity is only one-half cm. shorter than the other, which is quite within the normal limits of variation.

Case 2. This boy of 11 years is a case of congenital hypertrophy of the foot. I have never before seen a case where the foot alone and not the leg was involved. Sometimes we have hypertrophy of the toes or fingers, but hypertrophy of the foot is very uncommon. The mother is said to have had a severe cellulitis of the foot during pregnancy. An interesting fact in this connection is that every three or four months the patient has what appears to be an inflammation in the foot. One might think it was a case of beginning acromegaly, but I do not believe it is anything but a pure congenital hypertrophy of the foot. The patient can walk and run and has no tenderness, limitation of motion, or indication of a local disease in the foot or ankle.

Case 3. This little girl, about 8 years of age, has a congenital amputation of the forearm just below the elbow. She has two teat-like rudimentary fingers. The extreme upper end of the radius is of full size, while the ulna is rudimentary and can scarcely be felt. The rudimentary forearm is quite useful, enabling her to wash dishes and perform other household duties.

Case 4. This boy, 6 years of age, had a testicle incarcerated between the internal and external rings, both rings being tightly closed. The testicle was frequently bruised and painful. The people at one of the hernia institutes were anxious to inject him for the cure of a supposed hernia. The boy came into the Garrett Hospital, where I operated upon him. I exposed the testicle, and after stripping the cord up to the internal ring and making slow traction, succeeded in lengthening it sufficiently to reach the upper part of the scrotum; then by dilating the external ring from below it was made large enough to get the testicle through. The testicle was stitched to the bottom of the inverted scrotum and pulled down. It is now in the upper part of the scrotal pouch.

Case 5. This was a case of complete epispadias. The boy had only a trough out of which the urine dribbled day and night. I have performed upon him the five classical operations of Thiersch, which have spread over a long period of time. The result is very good. There was at first absolutely no closed urethra. He has now a complete urethra (with two small lateral openings, which will be closed later), through which he passes his water, and has very good power of control over his urine.

NOTES ON NEW BOOKS.

Dose-Book and Manual of Prescription-Writing, with a list of the official drugs and preparations, and also many of the newer remedies now frequently used, with their doses. By E. Q. THORNTON, M. D., Ph. G. (*Philadelphia: W. B. Saunders*, 1895.)

In the preface to this book the author states that his aim "has been to compile a work of value to the student of medicine both during his years of study as an undergraduate and in the early period of his professional career. The volume may also prove of value to the practitioner of many years standing for purposes of reference." Success in the effort to meet the requirements of two classes of persons in one volume is not easy of attainment, and is indeed possible only by making the book larger than would otherwise be necessary. Judged as a book of reference for the practitioner, Dr. Thornton's work is excellent, though portions are more elementary than is required for such use. To judge of it as a manual for the beginner a different standard must be adopted, because the latter in certain branches of the subject needs concise rules which he can remember instead of a systematic treatise, while in other branches the beginner, and he alone, requires full directions and suggestions. It is a common complaint that existing works on prescription-writing are not adapted to the beginner; and, as there is a demand for something better, the following comments on the manual in hand are made with a view to its usefulness in that direction.

Although in general this book is an improvement on its predecessors in the same field, it lacks the originality and independence of precedent which are necessary to the making of an ideal student's manual. Part I, on Weights and Measures, English and metric, is clearly and thoroughly written, but the impression is given throughout that the metric system is used as a translation from the English. Of course gr. xv equals ".9720 Gm." and one drachm equals "3.9 Gm.", but is dosage ever so exact as to require the use of such fractions? As the physician never orders $2\frac{1}{4}$ drachms as a dose, why should he order 7.776 grammes? If the metric system is to come into general use (as it surely will), we must think in its units and not attempt to remember long decimals.

The twelve pages on prescription-writing and the four on principles of medical combination are excellent, so far as they go, but some of the paragraphs ought to be expanded into chapters, as the student finds his greatest difficulty in combining drugs in extemporaneous prescriptions. Prescription Latin, on the other hand, might profitably be condensed to its simplest rules instead of filling twenty-six pages. The sections on Incompatibilities and Solubilities are unusually good for reference purposes, but one looks in vain for a few general rules which the student can always bear in mind.

Part III, Official Preparations and Methods of Prescribing, is the most original part of the book and is full of useful suggestions, albeit the author has forgotten to include the oils in his thirty-nine preparations. The remainder of the volume, almost one half, has an air of padding to fill a required number of pages. Every text-book on materia medica contains a dose list, and the catalogue of drugs here given has no new feature to commend it to the student. Under a different arrangement, the lists of official preparations in the preceding part are duplicated. One of the chief errors of writers on this subject is to suppose a complete catalogue of drugs is needed by the beginner. In fact, such list is of value only as supplying a mass of material from which to select, and is wholly indigestible unless the student already knows how to gather the most useful articles from it. What, for example, is to guide him in choosing between the tincture, aromatic tincture, sweet tincture, fluid extract, syrup, and aromatic syrup of rhubarb? Is the young doctor expected to follow the list seriatim when he prescribes rhubarb, or is he to decide by lot what to select from Dr. Thornton's catalogue? Again, it is of little importance to state the exact number of official oleoresins or to give a list of the many preparations of cubebs. The information needed is which of the oleoresins is of permanent value, and whether the beginner, in prescribing cubebs, had better select the oleoresin or the oil.

Knowledge of real value to the student, which might well be given in a manual of prescription-writing, is suggested by the following topics: The relative value of the various preparations; which of them are in constant and growing use; how to choose between them for forming combinations or to suit the patient's needs; general principles of the use of official remedies in preference to old but unofficial ones, on the one hand, and newly introduced drugs or Smith's or Brown's "superior preparations" on the other; the use of alkaloids or synthetic carbon compounds in preference to crude vegetable products. A statement, respecting each valuable drug, of its best solid and liquid preparations for general use might well be added, and also a list of the best diluents, excipients and flavoring agents, with directions for the use of each.

Of the need for a complete, accurate work on this subject there can be but one opinion. The young physician has no more important duty than the correct writing of the best prescriptions he can devise, and everything that enables him to excel in this task is not only an aid in his professional advancement, but is, to his patients, directly health-saving and life-saving.

ANITA NEWCOMB MCGEE.

Part I. Essentials of Refraction and the Diseases of the Eye. By EDWARD JACKSON, A. M., M. D., Professor of Diseases of the Eye in the Philadelphia Polyclinic and College for Graduates in Medicine, Member of the American Ophthalmological Society, etc., etc.

Part II. Essentials of Diseases of the Nose and Throat. By E. B. GLEASON, S. B , M. D., Surgeon in Charge of the Nose, Throat and Ear Department of the Northern Dispensary of Philadelphia; formerly Assistant in the Nose and Throat Dispensary of the Hospital of the University of Pennsylvania, etc., etc. Second Edition Revised; 124 illustrations. (*Philadelphia: W. B. Saunders*, 1894.)

This compend is meant for those postgraduate students who are trying to get a better working knowledge of the diseases of the eye, and to help the general practitioner who is not satisfied with his knowledge of diseases of the eye, but desires to learn how to treat intelligently the most common eye affections and at the same time to recognize the point where the disease demands a specialist's attention. To aid in this direction we think the book is well adapted. The questions are sensibly framed and clearly answered. The chapter on diseases of the conjunctiva is particularly good, but in speaking of the treatment of purulent ophthalmia, we think it would have been well had the author stated just how much of the solution of nitrate of silver should be used at each application, for we know of more than one case where too much zeal in its use in purulent ophthalmia has been followed, it is true, by the disappearance of the ophthalmia, but also by permanently clouded corneæ, from the effects of the chemical. The illustrations, 52 in number, are taken generally from the more complete works on ophthalmology. The author certainly has reason to hope that those who go further in the science of ophthalmology will find in his Essentials "a good foundation for future progress."

The work on diseases of the nose and throat contains all that is of practical value to the postgraduate student. We see no reason why these two subjects, so remote from one another, should be associated as they are in one volume.

Essentials of the Diseases of the Ear. Arranged in the form of Questions and Answers. Prepared especially for Students of Medicine and Postgraduate Students. By E. B. GLEASON, S. B., M. D., Clinical Professor of Otology, Medico-Chirurgical College, Philadelphia. (*Philadelphia: W. B. Saunders*, 1894.)

The author has gotten together in an attractive form practically all that is useful in otology. Text-books on the ear are not satisfactory reading, to say the least, to the general practitioner, but we think the latter will find the "Essentials," generally speaking, free from what is tiresome, and really helpful in his postgraduate work.

BOOKS RECEIVED.

Diseases of the Female Bladder and Urethra. By Howard A. Kelly. Baltimore. Pamphlet.

Transactions of the College of Physicians of Philadelphia. V. 16. 8vo. 287 pages. 1894. Philadelphia.

Heredity, Health and Personal Beauty. By John V. Shoemaker, A. M., M. D. 8vo. 422 pages. 1890. F. A. Davis, Philadelphia.

Essentials of Diseases of the Ear. By E. B. Gleason, S. B., M. D. (Saunders' Question-Compends.) 12mo. 147 pages. 1894. W. B. Saunders, Philadelphia.

Essentials of Diseases of the Eye, Nose and Throat. By Edward Jackson, A. M., M. D., and E. B. Gleason, S. B., M. D. (Saunders' Question-Compends.) 12mo. 290 pages. 2d ed. 1894. W. B. Saunders, Philadelphia.

Two Monographs on Malaria and the Parasites of Malarial Fevers. I. Marchiafava and Bignami. II. Mannaberg. 8vo. 428 pages. 1894. The New Sydenham Society, London.

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